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A Review on Insomnia and its Management

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Abstract

Insomnia disorder is a common problem where individuals experience difficulty sleeping, impacting their daily lives and decreasing enjoyment. However, the occurrence of insomnia disorder, which can be either acute short term or chronic long lasting. This article provides an overview of insomnia and its management. The primary causes, risk factors and epidemiology associated with insomnia are outlined, along with the criteria for making a precise diagnosis. The management of insomnia, typically involving a combination of cognitive behavioral therapy and pharmacological treatment are discussed.

Keywords; Insomnia disorder, sleep, cognitive behavioral therapy, pharmacological management.

Introduction

Sleep is crucial for brain development learning, memory, emotional balance, heart and metabolism health and removing cell toxins. (1,2) A recent study indicates that about 25% of the adult population experiences sleeping disorder, and among those, approximately 6- 10% suffer from insomnia. (3) Sufficient sleep is essential for maintaining health and enhancing overall life satisfaction. Research indicates that lack of sleep and disturbances in the circadian rhythm can result in changes to immune function, along with a higher likelihood of developing cardiovascular issues and metabolic conditions like weight gain, insulin resistance, and diabetes. (1,4) Patients with insomnia experience decreased quality of life, worse daytime functioning, and higher risk of accidents. Insomnia frequently occurs alongside chronic health issues, mental health conditions such as depression and anxiety and metabolic disorders, or can occur as a consequence of these conditions. (5) The rising occurrence of insomnia and various sleep disorders, which are frequently underrecognized and inadequately treated, is a worldwide issue. (6)

Definition and types of sleep disorder

Insomnia is characterized by challenges in falling asleep or staying asleep, as well as waking up too early. This condition leads to diminished functioning during the day, which may manifest as decreased cognitive abilities, tiredness, or mood issues. (7)

The Third Edition of the International Classification of Sleep Disorders (ICSD-3) recognizes three specific categories of insomnia: short-term insomnia, chronic insomnia, and other insomnia (which refers to patients experiencing insomnia symptoms that do not fulfill the criteria for the other two categories). (7,8) The DSM-5 has eliminated the distinction between "primary" and "secondary" insomnia and now recognizes insomnia as a standalone disorder when criteria for both nighttime and daytime symptoms are fulfilled, regardless of any co-occurring condition. (9) Recently, the international classification of sleep disorders, third edition (ICSD-3) has shifted to describing insomnia through a broader and more inclusive concept known as "insomnia disorder." (7) A new overarching category, called 'insomnia disorder', has been established and is also included in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM–5). (8)

Epidemiology

Sleeplessness is a common issue that can impact individuals of all ages, including kids, adults, and seniors. (10,11) Roughly a third of adults occasionally experience sleep issues, while 6–10% describe symptoms that fit the diagnostic criteria for insomnia disorder. (12) The prevalence of insomnia varies significantly based on the criteria used and whether it is viewed as a symptom of a different disorder or as a standalone issue. Often, insomnia is recorded as a coexisting condition associated with another medical or mental health disorder. For instance, approximately 50% of people experiencing insomnia symptoms will also show signs of another psychiatric condition. (9) Insomnia is also a risk factor for comorbid medical and psychiatric disorders, including anxiety and depression. (13,14) The prevalence of insomnia is inconsistently reported in the scientific literature, due to different perceptions of insomnia and its treatment amongst patients and clinicians. (15)

Main causes and risk factors

Risk factors for developing insomnia encompass having experienced an episode of insomnia in the past, a family history of insomnia, and a tendency to awaken more easily from sleep. (10,16,17) Environmental causes of insomnia include noise, temperature, light, electronic devices and uncomfortable sleeping positions. (11) Substance abuse and dependence on cocaine, alcohol, nicotine and codeine contribute to insomnia. (18) The aging process is a major contributor to alterations in sleep patterns. (19) Health issues such as cancer, gastrointestinal disorders, respiratory illnesses, cardiovascular diseases, neurological conditions, and specific medications used to treat these ailments can disrupt sleep, resulting in insomnia.

(20) insomnia is prevalent in pregnant women possibly due to discomfort, depression and other pregnancy related complications. (17,18). Table I provides a summary of medicines that are associated with insomnia.

Table I. Pharmacological causes of insomnia (7,11,18)

Pharmacological class	Drug examples
α-blockers	Tamsulosin
β-blockers	Propranolol, metoprolol
β2-agonists	Salbutamol, salmeterol
Corticosteroids	Prednisone
Decongestants	Phenylephrine, pseudoephedrine
Diuretics	Furosemide, hydrochlorothiazide
Dopamine receptor agonists	Levodopa
Monoamine oxidase inhibitors (MAOIs)	Phenelzine, tranylcypromine
Selective serotonin reuptake inhibitors (SSRIs)	Citalopram, fluoxetine, sertraline, fluvoxamine
Central nervous system stimulants	Amphetamine, cocaine, ephedrine, caffeine, modafinil
Other	Phenytoin, nicotine, thyroid supplements, bupropion, venlafaxine, theophylline

Clinical characteristics and diagnosis

Diagnosis of insomnia

Insomnia represents a significant public health issue that necessitates precise diagnosis and efficient treatment. (21) The ICSD-3 is the most widely used classification system for sleep disorders, with diagnostic criteria for insomnia disorder summarised in table II. Insomnia is primarily a clinical diagnosis and is most frequently diagnosed using data obtained from patient histories and sleep diaries. (7,8,22)

Acute insomnia

Short-term insomnia is often aggravated by stressful situations and is therefore usually resolved when the underlying cause is resolved or when the patient develops coping mechanisms. (23) short term insomnia with sleep disruptions and effects during the day lasting less than three months typically arises from a triggering stressor, leading to a noticeable alteration in sleep quality. (9) Acute insomnia can potentially progress into chronic insomnia if people adopt altered perceptions and unhelpful habits concerning sleep. (24) diagnostic criteria for short term insomnia disorder table II (7,8,22)

Table II. ICSD-3 Diagnostic criteria for insomnia disorder (7,8,22)

A-E Criteria must be meet

A Patients rep
ort or the patient's parent/caregiver observes one or more of the following:

1. Difficulty initiating sleep
2. Difficulty maintaining sleep
3. walking up earlier than desired
4. Resistance to going to bed at an appropriate time
5. Difficulty sleeping without parent or caregiver intervention

B. Reports from patients or the patient's parent/caregiver detect one or more of the following, related to difficulty sleeping at night:

1. Fatigue/discomfort
2. Impaired attention, concentration or memory
3. social, family, professional or academic development impairment
4. Mood disturbance/irritability
5. Daytime sleepiness
6. Behaviour problems (e.g., hyperactivity,impulsivity,aggression)
7. Reduced motivation/energy/initiative

8. Predisposition for errors/accident
9. Concerns/dissatisfaction with sleep

C. Sleep/wake complaints cannot be explained solely by an inadequate opportunity for sleep (insufficient time is allocated for sleep) or inadequate circumstances (the environment is not safe, dark, quiet and comfortable) for sleep

D. Sleep disturbance and associated daytime symptoms are present for less than three months.

E. Sleep/wake difficulty is not better explained by another sleep disorder.

Chronic insomnia

In order to fulfil the diagnostic requirements for chronic insomnia disorder, the individual must experience symptoms a minimum of three times weekly for a period of three months or longer. (7,22,25) Chronic insomnia, also known as insomnia disorder, is characterized by difficulty sleeping that occurs at least three nights a week for a duration of three months, leading to considerable distress or disruption in daytime activities. Chronic insomnia, or insomnia disorder, is characterized by difficulties in sleep that happen three or more nights weekly over a period of three months, resulting in significant distress or negative effects on daytime performance. (9) Nevertheless, there are instances where this can progress into long-term insomnia. (7,25) In a long-term study involving 388 individuals suffering from chronic insomnia, 46% of participants continued to experience ongoing symptoms after three years, while 14% experienced a relapse after their insomnia had previously improved. (26) The likelihood of experiencing insomnia again is quite high, making a previous occurrence of insomnia a key indicator for the potential onset of insomnia disorder in the future. (27)

Comorbidities

Co-occurring disorders like depression, anxiety, and long-term medical issues are prevalent. (28) Insomnia often occurs alongside psychological or physical conditions, other sleep issues, or the use of particular medications or substances. (18,20) Since insomnia and associated conditions can influence one another, it is crucial to thoroughly assess and manage all underlying issues.

Additionally, insomnia might occur alongside another sleep disorder. As many as 50% of individuals with obstructive sleep apnea may experience insomnia symptoms and may struggle with adhering to continuous positive airway pressure (CPAP) therapy. (29) In some case, treatment with cognitive behavioural therapy for insomnia has offered improvement to co-morbid conditions e.g. depression or chronic pain. (17) Examples of conditions and disorders that may coexist with insomnia are shown in Table III.

Clinical features

The primary symptoms associated with insomnia include tiredness, increased irritability, difficulties in social interactions, issues with focus or memory, a decrease in motivation, heightened aggression, and anxiety regarding sleep, which can result in diminished performance during the day and potentially lead to accidents or mistakes.(7,30) Patients with chronic insomnia frequently report a sense of reduced alertness and a desire for sleep, but inability to sleep and achieve the relief they seek. (21,30,31)

Table III. Common co-morbid conditions and disorders associated with Insomnia (16,18,32,33,34)

Type of condition	Examples of conditions or disorders
Endocrine	Diabetes mellites, hyperthyroidism, hypothyroidism
Cardiovascular	Angina, congestive heart failure, dysrhythmias
Renal and urinary	Incontinence, nocturia, enuresis, chronic kidney
Psychiatric	Depression, generalised anxiety disorder, panic disorder, post-traumatic stress disorder, schizophrenia, Alzheimer's disease, attention-deficit hyperactivity disorder
Musculoskeletal	Rheumatoid arthritis, osteoarthritis, fibromyalgia
Neurological	Stroke, dementia, Parkinson's disease, seizure, headache, traumatic brain injury, peripheral neuropathy, chronic pain disorders, neuromuscular disorders
Reproductive	Pregnancy, menopause
Sleep	Sleep apnoea, restless legs syndrome, circadian rhythm sleep disorders, parasomnias

other	Allergies, rhinitis, sinusitis, chronic obstructive pulmonary disorder

Management of Insomnia

Improving both the quantity and quality of sleep, lowering the anxiety and suffering that comes with inadequate sleep, and enhancing daytime functioning are all objectives of insomnia treatment. (32) Determining the underlying reason for insomnia should be the initial focus in addressing the condition. If it arises as a secondary effect of a psychiatric or medical issue, addressing these primary causes may help alleviate the insomnia. (33) A frequent method for addressing insomnia involves utilizing both cognitive behavioural therapy and medication. (32) If insomnia is addressed early on, it may be possible to prevent the development of more complicated sleep-related disorders. Conversely, if insomnia goes untreated, recurring episodes can lead to chronic and stubborn insomnia. If this condition persists over a long period, the individual may develop a pattern of psychophysiological (conditioned) insomnia, where the sleep issues become ingrained psychologically and physiologically, making them increasingly challenging to resolve. (34) In all patients, the underlying causes of insomnia and any potential coexisting disorders should be determined as a component of the management plan. (35) The selection of insomnia treatment also relies on the symptoms exhibited and their intensity, the anticipated length of the treatment, any coexisting conditions, the patient's readiness to participate in behavioural therapies, and their susceptibility to potential side effects from medications. (19)

Non-pharmacological management: cognitive behavioral therapy

It has been demonstrated that non-pharmacological treatment of insomnia is an effective first-line treatment for people with persistent insomnia**.** (36,37) CBT-I is a comprehensive approach, and in the setting of clinical trials, it enhances sleep in 70% of individuals with insomnia. (13,38) Cognitive behavioural therapy for insomnia (CBT-i) enhances sleep results with few negative effects and is favoured by patients over medication treatment. (39) CBT-i components include sleep hygiene education, cognitive therapy, relaxation therapy, stimulus-control therapy and sleep-restriction therapy. (Table IV). (40) Studies have demonstrated that CBT-i is more effective than hypnotic medications and comes with fewer side effects. (12,18) For patients who do not see improvement from brief behavioural therapy, cognitive therapies for insomnia might be necessary. It may be beneficial to refer them to a sleep psychologist. Cognitive behavioural therapy has been shown to be an effective long-term solution, with a meta-analysis indicating notable enhancements in sleep onset latency and sleep efficiency lasting up to 12 months.(39) When implementing CBT-i, it is crucial to also address any underlying medical and psychiatric conditions to enhance sleep improvements.(12) Since CBT-i is suggested as the primary treatment for insomnia, upcoming challenges involve enhancing its visibility and availability for patients.(12,18)

Table IV. Components of cognitive behavioral therapy for insomnia (40)

Components	Rationale	Direction
Sleep hygiene	Encourages positive nighttime routines and creates an optimal setting for rest	Behaviours: • Avoid caffeine and nicotine before bedtime • Maintain a regular bed and wake time •Take regular daytime exercise Environment; • Maintain bedroom as a place to sleep • Reduce noise and light • Control temperature • Avoid bedroom clutter
Sleep/time in bed restriction	strives to align the projected total sleep duration with the chances to rest. This minimizes the excessive time spent awake in bed and enhances both sleep drive and sleep debt, leading to better sleep consolidation on following nights.	Evaluate the patient's natural sleepiness and their approximate total sleep duration during the night (keeping a sleep diary can be beneficial in this context). Set a regular bedtime and wake-up time based on the estimated total sleep duration, ensuring at least six hours of sleep opportunity, with a goal of no more than 30 minutes of wakefulness. Stick to a uniform sleep-wake schedule regardless of the actual sleep achieved overnight. Gradually extend the sleep opportunity in 30-minute increments during follow-up assessments based on the patient's progress.

Stimulus control	Promotes a consistent sleep–wake schedule and reduces conditioned response around sleep	Avoid naps during the day to increase natural homeostatic sleep drive Only go to bed when sleepy. If unable to fall asleep or waking for prolonged periods during the night, engage in another activity. Only return to sleeping position or bed when sleepy.
Relaxation strategies	Aim to reduce hyperarousal that often underpins insomnia and to improve stress management	Meditation Breathing exercises Progressive muscle relaxation Guided visualisation practices Implement short relaxation periods at various times during the day.
cognitive therapy	Encourages thought restructuring around sleep and promotes mindfulness.	Challenge unhelpful beliefs and attitudes around sleep including the requirement for a certain number of hours of sleep, the health impacts of insomnia and attributional biases attached to inadequate sleep.

Pharmacological management

When addressing insomnia, pharmacological treatment options should be evaluated after thoroughly considering the advantages and disadvantages of treating the condition compared to not treating it. (37) At present, there are various medications available for the treatment of insomnia. Frequently used categories of drugs for managing insomnia include benzodiazepine receptor agonists (which encompass both non-benzodiazepines and benzodiazepines), melatonin receptor agonists, and the off-label use of antipsychotics, sedating antidepressants, and antihistamines like diphenhydramine. (41) The addition of medication to CBT-i in patients with persistent insomnia has been shown to produce added benefits during acute therapy, but with long-term treatment the outcome is optimised when medication is discontinued during maintenance CBT-i. (20) When pharmacological treatment is deemed necessary, the selection of medication is influenced by multiple factors, such as symptom patterns, desired treatment outcomes, previous responses to treatment, patient preferences, cost considerations, the availability of alternative treatments, co-existing health conditions, contraindications, interactions with other medications, and the

likelihood of adverse effects.(42) Of-label use of non-prescription medicines e.g. antihistamines, is a common practice in the management of insomnia.(43)

Benzodiazepine receptor agonist hypnotics

It encompasses both benzodiazepines (BDZ) and non-benzodiazepine receptor agonist hypnotic derivatives. The primary pharmacological agents utilized for treating insomnia are benzodiazepine receptor agonists, which are the oldest in this category. (44) Non-benzodiazepine receptor agonist hypnotics, often referred to as "Z" drugs, were developed later. Both categories of medications operate using the same basic mechanism of action. However, the newer non-benzodiazepine receptor agonist hypnotics have distinct pharmacodynamic properties that enhance their safety and tolerability (45)

Zaleplon

Zaleplon has a quick onset of action and a very short duration, making it an effective option for treating sleep-onset insomnia.

Eszopiclone

Eszopiclone is a non-benzodiazepine sedative derived from Pyrrolopyrazine. While its exact mechanism of action is not fully understood, it is thought to influence GABA receptors at binding sites that are either close to or allosterically linked to benzodiazepine receptors.

Estazolam

Estazolam is a benzodiazepine with an intermediate duration of action, characterized by a gradual onset and extended effects. It is primarily utilized for insomnia related to maintaining sleep.

Selective melatonin receptor agonist

A 2 mg extended-release formulation of melatonin is effective for treating insomnia in adults aged 55 and older over a duration of 13 weeks.(46)

Ramelteon was launched in 2005. It acts as a selective agonist for the melatonin MT1 and MT2 receptors. This medication was regarded as a significant breakthrough in insomnia treatment due to its unique mechanism of action. The MT1 and MT2 receptors are predominantly found in the suprachiasmatic nucleus (SCN) of the hypothalamus.(47) Ramelteon has demonstrated effectiveness in enhancing sleep during the initial phase of the sleep cycle. Additionally, it might help regulate the timing of the circadian system, thereby increasing the likelihood of feeling sleepy consistently at bedtime.(48)

5-HT2A receptor antagonists and related compounds

Research has shown that medications exhibiting antagonistic activity on postsynaptic 5-HT receptors are linked to sedation, and some of these can enhance the duration of slow wave sleep. Medications such as

mirtazapine and trazodone induce this effect and may be utilized in the treatment of insomnia; however, they are not currently approved for this purpose. Since these drugs affect multiple receptors, they are associated with a wide range of side effects, which limits their usage for this condition. (49)

Orexin antagonists

The excitatory neuropeptides known as "orexins" or "hypocretins" originate from neurons in the lateral hypothalamus and have extensive projections to various areas of the brain. Several studies have shown that there is a deficiency of orexins in the sleep disorder narcolepsy, which emphasizes the role of these compounds in supporting wakefulness. It has been proposed that if low levels of orexin are linked to excessive drowsiness, then reducing orexin activity could encourage sleep, at least for certain individuals suffering from insomnia. (50) Table V provides a summary of the pharmacological treatment options for the management of insomnia.

Table V. Pharmacological management of insomnia (19,32,36,51,52,53)

Pharmacological class	Drug examples	Indications
Benzodiazepine receptor agonist	Flunitrazepam (Hypnor®) Brotozolam (Lendormin®) Triazolam (Halcion®) Loprazolam (Dormonoct®) Flurazepam (Dalmadorm®) Nitrazepam (Arem®) *Quazepam (Doral®) Temazepam (Normison®) Lorazepam (Ativan®)	These are preferred very brief courses. Longer-acting medications, such as flurazepam (with a half-life of 47–100 hours), help with maintaining sleep but are infrequently prescribed due to an increased likelihood of residual effects during the day. In contrast, triazolam has a shorter half-life (2.5 hours) and is utilized for addressing difficulties with falling asleep. Medications with intermediate half-lives, like temazepam (half-life of eight to ten hours), should be specifically used for patients experiencing problems with either sleep onset or sleep maintenance.
Non-benzodiazepines: also acting as receptor agonist	Zolpidem (Zolpihexal®, Zolnox®, Stilnox®, Nyxe®,	These medications are recommended as the primary treatment for acute insomnia

	Noxidem®, Medploz®, Ivedal®) Zopiclone (Zopigen®, Zopivane®, Z-dorm®, Imovane®, Alchera®, Adco-zopimed®, Lunesta®) *Zaleplon (Sonata)	characterized by difficulties in initiating sleep. They have a brief biological half-life, and drugs like zolpidem (with a half-life of 2.5 hours) and zaleplon (with a half-life of one hour) are suggested for managing sleep-onset insomnia.
Orexin receptor antagonist	*Suvorexant (Belsomra®	The medication is a fairly recent option and is favoured for maintaining sleep as well as for addressing sleep-onset insomnia.
Melatonin receptor agonis	Melatonin (Circadin®)	this is beneficial for difficulty falling asleep without waking up during the night.
Tricyclic antidepressants	*Doxepin (Sinequan®, Silenor®	Doxepin improves sleep efficiency.
Antihistamines	Diphenhydramine (Sleepeze®, Mypaid Night Pain®, Betasleep®) Doxylamine (Somnil®)	These are first-generation antihistamines that can be purchased without a prescription. They have sedative effects. These might be helpful for those who struggle to fall asleep and experience multiple awakenings during the night.
Off-label medicines	Antidepressants: Trazodone (Molipaxin®) Mirtazapine (Remeron) Antiepileptic drugs: Gabapentin (Neurontin®) Pregabalin (Lyrica®)	Antidepressants are prescribed for individuals with specific co-existing conditions and are administered at reduced doses. Antiepileptic medications are utilized for managing insomnia in certain patients who have conditions like generalized anxiety disorder, chronic pain, epilepsy, and a background of substance abuse.
Herbal treatments	Valerian Kava Chamomile	Herbal treatments have calming properties, which is why they are utilized. However, there is

		inadequate evidence to confirm the effectiveness of these herbal single preparations in treating insomnia, and there is limited proof indicating that they are a safe and well-tolerated option for patients suffering from insomnia.

Conclusion

In conclusion, the impact of insomnia is considerable and can adversely affect a person's overall health. Even though it is common, insomnia is often not diagnosed or treated adequately. Long-term insomnia has been linked to an increased likelihood of developing chronic illnesses, making it essential to recognize and address the underlying factors. The preferences and values of the patient must be taken into account when choosing treatment alternatives. Hypnotic medications should be prescribed for the briefest duration necessary and at the minimal effective dose to prevent the risk of dependence and tolerance. The treatment of insomnia involves medication, cognitive behavioral therapy, and addressing any co-existing conditions. The primary aim of therapy is to enhance the quality and duration of sleep, boost daytime functioning, and lower anxiety levels. Depending on how severe the insomnia is, cognitive behavioral therapy and medication may be utilized separately or together, although behavioral therapy is typically advised as the first line of treatment.

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